

=> d his

(FILE 'HOME' ENTERED AT 13:30:24 ON 12 SEP 2005)

FILE 'CAPLUS' ENTERED AT 13:30:35 ON 12 SEP 2005

L1 1 S US6645950/PN  
SELECT L1 1 RN  
L2 11712 S E1-E35

FILE 'REGISTRY' ENTERED AT 13:31:38 ON 12 SEP 2005

L3 1 S 209803-68-9/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

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L4 1 S 15761-38-3/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:32:13 ON 12 SEP 2005

L5 1 S 29178-60-7/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:32:45 ON 12 SEP 2005

L6 1 S 56073-91-7/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:35:29 ON 12 SEP 2005

L7 1 S 34840-23-8/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:35:55 ON 12 SEP 2005

L8 1 S 56073-96-2/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:36:42 ON 12 SEP 2005

L9 1 S 72447-64-4/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 13:40:24 ON 12 SEP 2005

L10 1 S 93958-45-3/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

L11 29 S E4-E26, E29-E34

FILE 'CAPLUS' ENTERED AT 13:42:06 ON 12 SEP 2005

L12 43 S L11  
L13 1 S L12 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO?)

FILE 'USPATFULL, USPAT2' ENTERED AT 13:47:35 ON 12 SEP 2005

L14 4 S L12  
L15 3 S L14 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO?)

FILE 'CAPLUS' ENTERED AT 13:57:47 ON 12 SEP 2005

L16 1 S L12 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO? OR PROLI

FILE 'REGISTRY' ENTERED AT 14:00:11 ON 12 SEP 2005

L17 1 S 56073-98-4/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'EPFULL, FRFULL, GBFULL, PATDPAFULL, PCTFULL, RDISCLOSURE,

USPATFULL, USPAT2' ENTERED AT 14:07:11 ON 12 SEP 2005  
L18 3 S L16

FILE 'MEDLINE' ENTERED AT 14:08:53 ON 12 SEP 2005  
L19 0 S L18  
L20 0 S L12 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO? OR PROLIF

FILE 'CAPLUS' ENTERED AT 14:12:32 ON 12 SEP 2005  
L21 2 S L20

FILE 'USPATFULL, USPAT2' ENTERED AT 14:13:09 ON 12 SEP 2005  
L22 3 S L20

FILE 'MEDLINE' ENTERED AT 14:15:45 ON 12 SEP 2005  
L23 408 S (HELMINTH? OR ANTHELMINT?) (L) (CANCER? OR TUMOR? OR NEOPLAST?  
L24 225 S L23 NOT PY>=1999  
L25 173 S (HELMINTH? OR ANTHELMINT?) (L) (CANCER? OR TUMOR? OR NEOPLAST?  
L26 92 S L25 NOT PY>=1999

=>

=> s us6645950/pn  
L1 1 US6645950/PN

=> select l1  
ENTER ANSWER NUMBER OR RANGE (1-):1  
ENTER DISPLAY CODE (TI) OR ?:rn  
E1 THROUGH E35 ASSIGNED

=> s e1-e35

8785 103-71-9/BI  
89 117924-33-1/BI  
2663 15761-38-3/BI  
3 209803-68-9/BI  
1 284019-29-0/BI  
1 284019-30-3/BI  
1 284019-31-4/BI  
1 284019-34-7/BI  
1 284019-36-9/BI  
1 284019-39-2/BI  
1 284019-41-6/BI  
1 284019-43-8/BI  
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1 284019-55-2/BI  
1 284019-56-3/BI  
1 284019-57-4/BI  
1 284019-58-5/BI  
1 284019-59-6/BI  
5 29178-60-7/BI  
175 34840-23-8/BI  
5 56073-91-7/BI  
6 56073-92-8/BI  
5 56073-95-1/BI  
13 56073-96-2/BI  
4 56073-98-4/BI  
27 72447-64-4/BI  
2 93958-45-3/BI

e4

e26

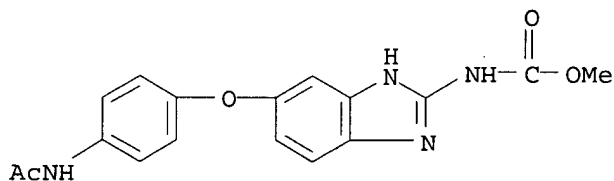
e29

e34

e4-e26  
e29-e34

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9-34-7/BI OR 284019-36-9/BI OR 284019-39-2/BI OR 284019-41-6/BI  
OR 284019-43-8/BI OR 284019-44-9/BI OR 284019-46-1/BI OR 284019-  
47-2/BI OR 284019-48-3/BI OR 284019-49-4/BI OR 284019-50-7/BI  
OR 284019-51-8/BI OR 284019-52-9/BI OR 284019-53-0/BI OR 284019-  
55-2/BI OR 284019-56-3/BI OR 284019-57-4/BI OR 284019-58-5/BI  
OR 284019-59-6/BI OR 29178-60-7/BI OR 34840-23-8/BI OR 56073-91-  
7/BI OR 56073-92-8/BI OR 56073-95-1/BI OR 56073-96-2/BI OR 56073  
-98-4/BI OR 72447-64-4/BI OR 93958-45-3/BI)

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 56073-91-7 REGISTRY  
CN Carbamic acid, [5-[4-(acetylamino)phenoxy]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C17 H16 N4 O4  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)  
DT.CA Caplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

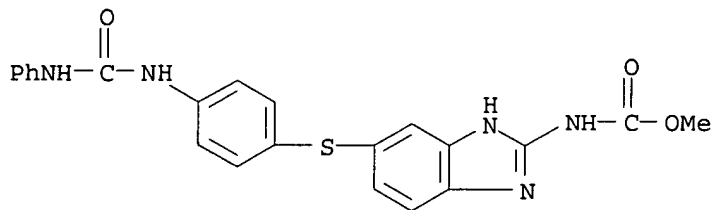


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1907 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

*Instant  
Compound*

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 209803-68-9 REGISTRY  
CN Carbamic acid, [5-[[4-[[[(phenylamino)carbonyl]amino]phenyl]thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H19 N5 O3 S  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA Caplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

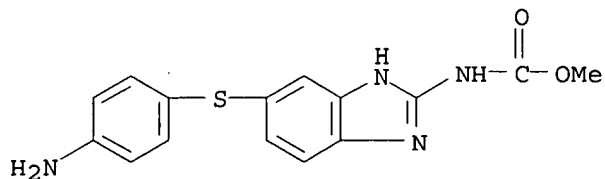


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

*instant  
Compound*

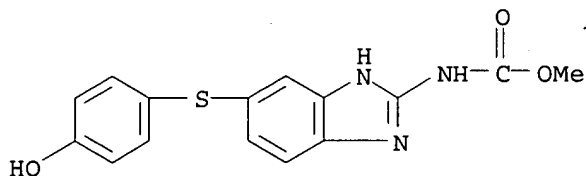
L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 56073-96-2 REGISTRY  
CN Carbamic acid, [5-[(4-aminophenyl)thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C15 H14 N4 O2 S  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)  
DT.CA Caplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

13 REFERENCES IN FILE CA (1907 TO DATE)  
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

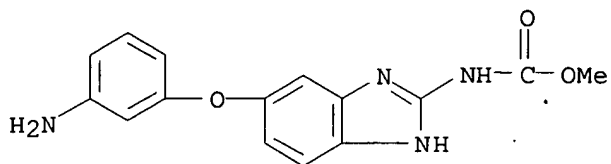
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 72447-64-4 REGISTRY  
 CN Carbamic acid, [5-[(4-hydroxyphenyl)thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN HOE 2542  
 CN p-Hydroxyfenbendazole  
 FS 3D CONCORD  
 MF C15 H13 N3 O3 S  
 LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, DDFU, DRUGU, MEDLINE, TOXCENTER, USPATFULL, VETU  
 DT.CA Caplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); PRP (Properties); USES (Uses)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

27 REFERENCES IN FILE CA (1907 TO DATE)  
 27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 56073-98-4 REGISTRY  
CN Carbamic acid, [5-(3-aminophenoxy)-1H-benzimidazol-2-yl]-, methyl ester  
(9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C15 H14 N4 O3  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER,  
USPATFULL  
(\*File contains numerically searchable property data)  
DT.CA Caplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)  
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)



=> d ibib 1-3

L15 ANSWER 1 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2004:108181 USPATFULL  
TITLE: Chemical compounds  
INVENTOR(S): Cheung, Mui, Durham, NC, UNITED STATES  
Harris, Philip Anthony, Durham, NC, UNITED STATES  
Hasegawa, Masaichi, Tsukuba-shi, JAPAN  
Ida, Satoru, Keita, JAPAN  
Kano, Kazuya, Tsukuba-shi, JAPAN  
Nishigaki, Naohiko, Tsukuba-shi, JAPAN  
Sato, Hideyuki, Tsukuba-shi, JAPAN  
Veal, James Marvin, Apex, NC, UNITED STATES  
Washio, Yoshiaki, Tsukuba-shi, JAPAN  
West, Rob I., Stevenage, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004082583	A1	20040429
APPLICATION INFO.:	US 2003-433128	A1	20031112 (10)
	WO 2001-US44553		20011128
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398		
NUMBER OF CLAIMS:	95		
EXEMPLARY CLAIM:	1		
LINE COUNT:	5806		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2004:77193 USPATFULL  
TITLE: Benzimidazole vascular damaging agents  
INVENTOR(S): Davis, Peter David, Watlington, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004058972	A1	20040325
APPLICATION INFO.:	US 2003-612163	A1	20030703 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-889061, filed on 22 Oct 2001, GRANTED, Pat. No. US 6645950		

*instant application*

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-752	19990115
	WO 2000-GB99	20000114
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PATENT ADMINSTRATOR, KATTEN MUCHIN ZAVIS ROSENMAN, 525 WEST MONROE STREET, SUITE 1600, CHICAGO, IL, 60661-3693	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
LINE COUNT:	774	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2003:296918 USPATFULL  
TITLE: Benzimidazole vascular damaging agents  
INVENTOR(S): Davis, Peter David, Watlington, UNITED KINGDOM  
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., Oxfordshire, UNITED  
KINGDOM (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6645950	B1	20031111
	WO 2000041669		20000720

*parent case*

APPLICATION INFO.:       US 2001-889061               20011022   (9)  
                          WO 2000-GB99               20000114

	NUMBER	DATE
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PRIORITY INFORMATION:	GB 1999-752	19990115
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Stockton, Laura L.	
NUMBER OF CLAIMS:	6	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	731	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

ACCESSION NUMBER: 1995:295616 CAPLUS  
DOCUMENT NUMBER: 122:95971  
TITLE: Benzimidazoles, potent anti-mitotic drugs: substrates for the P-glycoprotein transporter in multidrug-resistant cells  
AUTHOR(S): Nare, Bakela; Liu, Zhi; Prichard, Roger K.; Georges, Elias  
CORPORATE SOURCE: Inst. Parasitology, McGill Univ., Anne de Bellevue, QC, H9X 3V9, Can.  
SOURCE: Biochemical Pharmacology (1994), 48(12), 2215-22  
CODEN: BCPA6; ISSN: 0006-2952  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

- AB P-glycoprotein is thought to mediate the energy-dependent efflux of many structurally and functionally unrelated lipophilic compds. Presently, the mol. mechanism underlying the binding and efflux of drugs by P-glycoprotein is not well understood. However, it has been suggested that two planar benzene ring structures and a cationic charge are commonly found in many drugs that interact with P-glycoprotein. The benzimidazoles (BZs) are potent anti-tumor, anti-fungal and anti-parasitic agents, whose mode of action is thought to result from their inhibition of microtubule functions. Although other classes of microtubule inhibitors, such as colchicine and vinblastine, have been studied extensively with respect to their interaction and efflux by P-glycoprotein, the BZ group of drugs has not been characterized. In this study, the authors have characterized the interaction of BZ with multidrug-resistant cells and found that resistant cells accumulated substantially less BZ compared with drug-sensitive cells. Furthermore, BZ was more toxic to sensitive than to drug-resistant cells, suggesting that BZ is likely to be a substrate for the P-glycoprotein drug efflux pump. In addition, the authors used a photoactive analog of BZ ([125I]ASA-BZ) to demonstrate a direct binding between BZ and P-glycoprotein. Results showing that a molar excess of vinblastine, unmodified BZ, verapamil and rhodamine 123, but not colchicine, inhibited the photoaffinity labeling of P-glycoprotein by [125I]ASA-BZ confirmed the binding specificity of BZ to P-glycoprotein. Protease digestion of [125I]ASA-BZ photoaffinity labeled P-glycoprotein yielded two peptides that were similar to those obtained with other P-glycoprotein-associated drugs, e.g., azidopine and iodoaryl azidoprazosin. Taken together, these results demonstrate a direct and specific interaction between P-glycoprotein and BZ in a manner that is probably similar to other previously characterized P-glycoprotein-associated drugs.
- AB P-glycoprotein is thought to mediate the energy-dependent efflux of many structurally and functionally unrelated lipophilic compds. Presently, the mol. mechanism underlying the binding and efflux of drugs by P-glycoprotein is not well understood. However, it has been suggested that two planar benzene ring structures and a cationic charge are commonly found in many drugs that interact with P-glycoprotein. The benzimidazoles (BZs) are potent anti-tumor, anti-fungal and anti-parasitic agents, whose mode of action is thought to result from their inhibition of microtubule functions. Although other classes of microtubule inhibitors, such as colchicine and vinblastine, have been studied extensively with respect to their interaction and efflux by P-glycoprotein, the BZ group of drugs has not been characterized. In this study, the authors have characterized the interaction of BZ with multidrug-resistant cells and found that resistant cells accumulated substantially less BZ compared with drug-sensitive cells. Furthermore, BZ was more toxic to sensitive than to drug-resistant cells, suggesting that BZ is likely to be a substrate for the P-glycoprotein drug efflux pump. In addition, the authors used a photoactive analog of BZ ([125I]ASA-BZ) to demonstrate a direct binding between BZ and P-glycoprotein. Results showing that a molar excess of vinblastine, unmodified BZ, verapamil and rhodamine 123, but not colchicine, inhibited the photoaffinity labeling of P-glycoprotein by [125I]ASA-BZ confirmed the binding specificity of BZ to P-glycoprotein. Protease digestion of [125I]ASA-BZ photoaffinity labeled P-glycoprotein yielded two peptides that were similar to those obtained with other P-glycoprotein-associated drugs, e.g., azidopine and iodoaryl azidoprazosin.

IT

Taken together, these results demonstrate a direct and specific interaction between P-glycoprotein and BZ in a manner that is probably similar to other previously characterized P-glycoprotein-associated drugs.

**56073-98-4**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(benzimidazoles as potent anti-mitotic drugs and substrates for P-glycoprotein transporter in multidrug-resistant cells)